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Appendix G

Support for Claims 204 and 205 in the Instant ('191) Application

Disclosures:

Serial No.	Filing Date	Application family
09/265,191	3/10/99	CON of 08/593,554
08/593,554	1/30/96	CIP of 08/446,691

As the instant application is a continuation of the '554 application, support from the '554 is not detailed below. A pagination difference between the '191 and the '554 applications results in the page and line citations in the two applications being slightly different. The two applications contain the same content.

Claim #	Claim Limitation	Support in Applicants' Disclosure
204.	A method of treating an allergy in a vertebrate, ...	Page 4, lines 9-11: "The invention also includes naked gene expression vectors for use in manipulating cellular immune responses toward the TH1 compartment." Page 49, lines 9-10: "TH1 responses are to be of particular importance in the treatment of allergies and AIDS." Page 5, lines 13-15: "The vectors are also of particular use in stimulating the TH1 compartment in preference to the TH2 compartment, thus suppressing IgE production in response to expressed antigen [from the vector]." Page 36, lines 1-4: "Thus, administration of naked gene expression vectors which encode antigens (or known immunostimulatory fragments of antigens) according to the invention not only suppresses IgE antibody production, but also does so from the outset of therapy, thus avoiding the risk of anaphylaxis posed by conventional immunotherapy protocols." Page 50, line 6, to page 52, line 9: Example VII

Claim #	Claim Limitation	Support in Applicants' Disclosure
	...comprising administering to the vertebrate an effective amount of an immunostimulatory nucleic acid in a plasmid, ...	Page 49, line 1, to page 52, line 9: Examples VI & VII: Selective induction of Th1 response (VI) and suppression of IgE antibody response to antigen (VII) by immunization with antigen-encoding polynucleotides. Page 32, lines 22-23: "The host may be any vertebrate, but will preferably be a mammal."
	...said immunostimulatory nucleic acid comprising 5'CG3', wherein C is unmethylated, ...	Page 5, lines 16-18: "The naked gene expression vectors of the invention include one or more non-coding, immunostimulatory polynucleotides which include at least one dinucleotide sequence consisting of adjacent, unmethylated cytosine-guanine (CG) nucleotides."
	...and an effective amount of an antigen which stimulates production of allergy-associated IgE antibodies in the vertebrate, wherein said antigen is encoded in the plasmid.	Page 50, line 6, to page 52, line 9: Example VII: Suppression of IgE antibody response to antigen by immunization with antigen-encoding polynucleotides. Page 36, lines 1-4: "Thus, administration of naked gene expression vectors which encode antigens (or known immunostimulatory fragments of antigens) according to the invention not only suppresses IgE antibody production, but also does so from the outset of therapy, thus avoiding the risk of anaphylaxis posed by conventional immunotherapy protocols." Page 49, lines 6-8: "TH2 responses include the allergy-associated IgE antibody class; soluble protein antigens tend to stimulate relatively strong TH2 responses." Page 36, lines 13-17: "However, as demonstrated in Example VII, IgE antibody levels produced in the protein injected mice are substantially greater during the initial phase of treatment than are produced at any stage of treatment of mice injected with a naked gene expression vector (pCMV-LacZ) that operatively encodes the same antigen and includes an immunostimulatory polynucleotide of the invention (SEQ ID NO:1)."

Claim #	Claim Limitation	Support in Applicants' Disclosure
		Page 36, lines 22-24: "Moreover, the protection against IgE production afforded to the pCMV-LacZ challenged mice continues despite subsequent challenge with the plasmid or protein, even when combined with adjuvant (Examples IV, V and VII)." Page 34, lines 20-22: "In this embodiment, the TH1 component of the T lymphocyte immune response is generally stimulated in preference to the antigenic stimulation of TH2 lymphocytes, which mediate production of IgE antibody." Page 4, lines 9-11: "The invention also includes naked gene expression vectors for use in manipulating cellular immune responses toward the TH1 compartment." Page 5, lines 13-15: "The vectors are also of particular use in stimulating the TH1 compartment in preference to the TH2 compartment, thus suppressing IgE production in response to expressed antigen [from the vector]."

Claim #	Claim Limitation	Support in Applicants' Disclosure
205.	A method for suppressing an allergic response to an antigen...	Page 4, lines 9-11: "The invention also includes naked gene expression vectors for use in manipulating cellular immune responses toward the TH1 compartment." Page 49, lines 9-10: "TH1 responses are to be of particular importance in the treatment of allergies and AIDS." Page 5, lines 13-15: "The vectors are also of particular use in stimulating the TH1 compartment in preference to the TH2 compartment, thus suppressing IgE production in response to expressed antigen [from the vector]." Page 34, lines 20-22: "In this embodiment, the TH1 component of the T lymphocyte immune response is generally stimulated in preference to the antigenic stimulation of TH2 lymphocytes, which mediate production of IgE antibody." Page 36, lines 1-4: "Thus, administration of naked gene expression vectors which encode antigens (or known immunostimulatory fragments of antigens) according to the invention not only suppresses IgE antibody production, but also does so from the outset of therapy, thus avoiding the risk of anaphylaxis posed by conventional immunotherapy protocols." Page 36, lines 13-17: "However, as demonstrated in Example VII, IgE antibody levels produced in the protein injected mice are substantially greater during the initial phase of treatment than are produced at any stage of treatment of mice injected with a naked gene expression vector (pCMV-LacZ) that operatively encodes the same antigen and includes an immunostimulatory polynucleotide of the invention (SEQ ID NO:1)." Page 50, line 6, to page 52, line 9: Example VII

Claim #	Claim Limitation	Support in Applicants' Disclosure
	...in a mammal susceptible to an allergic reaction to said antigen which stimulates production of allergy-associated IgE antibodies in the mammal, ...	Page 32, lines 22-23: "The host may be any vertebrate, but will preferably be a mammal. Page 50, line 6, to page 52, line 9: Example VII: Administration of a plasmid of this invention suppressed antigen-specific IgE production (i.e., an allergic response) upon subsequent challenge with the antigen. Control animals in the experiment developed high levels of antigen-specific IgE. Page 36, lines 1-4: "Thus, administration of naked gene expression vectors which encode antigens (or known immunostimulatory fragments of antigens) according to the invention not only suppresses IgE antibody production, but also does so from the outset of therapy, thus avoiding the risk of anaphylaxis posed by conventional immunotherapy protocols." Page 36, lines 13-17: "However, as demonstrated in Example VII, IgE antibody levels produced in the protein injected mice are substantially greater during the initial phase of treatment than are produced at any stage of treatment of mice injected with a naked gene expression vector (pCMV-LacZ) that operatively encodes the same antigen and includes an immunostimulatory polynucleotide of the invention (SEQ ID NO:1)." Page 34, lines 20-22: "In this embodiment, the TH1 component of the T lymphocyte immune response is generally stimulated in preference to the antigenic stimulation of TH2 lymphocytes, which mediate production of IgE antibody." Page 49, lines 6-8: "TH2 responses include the allergy-associated IgE antibody class; soluble protein antigens tend to stimulate relatively strong TH2 responses."

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	...comprising parenterally administering to the mammal (a) an effective amount of an immunostimulatory nucleic acid in a plasmid, ...	Page 30, lines 6-9: "Parenteral vehicles include... Intravenous vehicles include..." See also page 33, lines 13-14 and page 40, lines 1-9. Page 49, line 1, to page 52, line 9: Examples VI & VII: Intradermal and intramuscular administration of antigen-encoding plasmids.
	...said immunostimulatory nucleic acid comprising 5'CG3', wherein C is unmethylated, ...	Page 5, lines 16-18: "The naked gene expression vectors of the invention include one or more non-coding, immunostimulatory polynucleotides which include at least one dinucleotide sequence consisting of adjacent, unmethylated cytosine-guanine (CG) nucleotides."

Claim #	Claim Limitation	Support in Applicants' Disclosure
	...and (b) an effective amount of the antigen or the antigen encoded in the plasmid.	Page 6, lines 18-21: "With co-administration of antigen or a recombinant expression vector encoding antigen, the naked gene expression vectors of the invention serve as adjuvants to enhance the immune response of a host to the antigen." Page 6, lines 1-4: "Given the immunostimulatory properties of the immunostimulatory polynucleotides of the invention, their inclusion in other recombinant gene expression vectors and antigen-based vaccine compositions can also be expected to enhance the anti-antigen immune response of the host." Page 37, lines 4-8: "The naked gene expression vectors of the invention may be used as adjuvants in conventional vaccination protocols or may be used in gene immunization protocols; i.e., where the target antigen is a protein antigen encoded by a naked gene expression vector (which may also be the vector that contains the non-coding, immunostimulatory polynucleotides of the invention)." Page 4, lines 9-11: "The invention also includes naked gene expression vectors for use in manipulating cellular immune responses toward the TH1 compartment." Page 5, lines 13-15: "The vectors are also of particular use in stimulating the TH1 compartment in preference to the TH2 compartment, thus suppressing IgE production in response to expressed antigen [from the vector]." Page 36, lines 22-24: "Moreover, the protection against IgE production afforded to the pCMV-LacZ challenged mice continues despite subsequent challenge with the plasmid or protein, even when combined with adjuvant (Examples IV, V and VII)." Page 50, line 6, to page 52, line 9: Example VII: Suppression of IgE antibody response to antigen by immunization with antigen-encoding polynucleotides.